

LISTING OF CLAIMS

1. *(currently amended)* A recombinant attenuated coxsackievirus B4 virion which is engineered to contain a heterologous nucleic acid inserted within the P1 region of the open reading frame of its genome which inserted nucleic acid encodes a heterologous polypeptide which is fused to a capsid protein of the virion.
2. *(withdrawn)* The recombinant attenuated coxsackievirus B4 virion of Claim 1 which is JVB.
3. *(previously presented)* The recombinant attenuated coxsackievirus B4 virion of Claim 1 which is a CB4-P virion.
4. *cancelled* — ~~The recombinant CB4-P virion of Claim 3 wherein the heterologous nucleic acid is inserted in the P1 region of the genome.~~
5. *cancelled*
6. *(currently amended):* The recombinant CB4-P virion of Claim 3 [[4]] wherein the heterologous polypeptide is situated within an immunogenic region of the viral capsid protein.
7. *(original):* The recombinant CB4-P virion of Claim 6 wherein the heterologous nucleic acid is expressed as an internal fusion of VP1.
8. *(original):* The recombinant CB4-P virion of Claim 6 wherein the viral capsid protein is VP1.
9. *(previously presented)* The recombinant CB4-P virion of Claim 8 wherein the immunogenic region of VP1 comprises a B-cell epitope, a T-cell epitope, or both a B cell epitope and a T cell epitope.
10. *(previously presented):* The recombinant CB4-P virion of Claim 8 wherein the heterologous polypeptide is situated within VP1 at a position which corresponds to the DE loop.
11. *(original):* The recombinant CB4-P virion of Claim 10 wherein the heterologous nucleic acid is directly downstream of codon 129 of VP1 coding sequences.
12. *(currently amended):* The recombinant CB4-P virion of Claim 11 wherein the heterologous nucleic acid replaces nucleic acid sequence[[s]] corresponding to VP1 codons 130-135 137 of wild type CB4-P is deleted.

13. (*currently amended*): The recombinant CB4-P virion of Claim 3 [[4]] wherein the heterologous nucleic acid is inserted in-frame and directly upstream of sequences which encode VP4, with the proviso that the insertion is optionally directly 3' from the AUG codon beginning at nucleotide 744 of the coxsackievirus B4 RNA genome that encodes the N-terminal Met of native viral polyprotein.

14. (*original*): The recombinant CB4-P virion of Claim 13 wherein the heterologous polypeptide is expressed as an amino-terminal fusion of the viral polyprotein.

15. (*original*): The recombinant CB4-P virion of Claim 14 wherein the amino-terminal fusion is susceptible to cleavage from the viral polyprotein by a viral protease.

16. ***cancelled***

17. (*previously presented*): The recombinant CB4-P virion of Claim 14 wherein the length of insert is from about 60 to about 360 nucleotides.

18. (*currently amended*) A nucleic acid comprising the complete genome of a recombinant attenuated coxsackievirus B4 virion which is engineered to contain a heterologous nucleic acid insert which is inserted within the P1 region of the open reading frame of its genome, wherein the insert encodes a heterologous polypeptide which in the virion is fused to a capsid protein.

19. (*withdrawn*): The nucleic acid of Claim 18 wherein the attenuated coxsackievirus is JVB.

20. (*original*): The nucleic acid of Claim 18 wherein the attenuated coxsackievirus is CB4-P.

21. (*original*): The nucleic acid of Claim 20 which is an infectious cDNA of the CB4-P genome.

22. (*original*): The nucleic acid of Claim 20 which is an infectious RNA of the CB4-P genome.

23. ***cancelled*** ~~The nucleic acid of Claim 20 wherein the insert is inserted into the P1 region of the genome.~~

24. (*currently amended*) The nucleic acid of Claim 20 [[23]] wherein the insert is in the coding region of VP1.

25. (*previously presented*) The nucleic acid of Claim 24 wherein the insert is in sequences which encode the DE loop of VP1.

26. (*previously presented*) The nucleic acid of Claim 25 wherein the insert is directly downstream of codon 129 of the VP1 coding sequences.
27. (*currently amended*) The nucleic acid of Claim 26 wherein the insert replaces nucleic acid sequence corresponding to VP1 codons 130-135 137 of wild type CB4-P VP1 coding sequences is deleted.
28. (*previously presented*): The nucleic acid of Claim 20 wherein the insert is in-frame and directly upstream of sequences which encode VP4, with the proviso that the insert is optionally 3' from the AUG codon, at nucleotide positions 744-746 of the coxsackievirus B4 RNA genome, that encodes the N-terminal Met of native viral polyprotein.
30. (*previously presented*): The nucleic acid of Claim 26 wherein the insert is from about 25 nucleotides to about 39 nucleotides in length.
31. (*previously presented*): The nucleic acid of Claim 26 wherein the polypeptide is immunogenic when fused to CB4-P VP1 capsid protein.
32. (*previously presented*): The nucleic acid of Claim 31 wherein the insert encodes a T cell epitope, a B cell epitope, or both a T cell epitope and a B cell epitope.
33. (*currently amended*): The nucleic acid of Claim 31 wherein the insert encodes a viral polypeptide or a peptide epitope fragment thereof.
34. (*currently amended*): The nucleic acid of Claim 31 wherein the insert encodes a polypeptide or a peptide epitope of a bacterial pathogen or a fragment thereof.
35. (*currently amended*): The nucleic acid of Claim 31 wherein the insert encodes an HIV polypeptide or a peptide epitope fragment thereof.
36. (*currently amended*): The nucleic acid of Claim 35 wherein the insert encodes HIV p24 or a peptide epitope fragment thereof.

37-53. Cancelled

54. (*withdrawn*): A method for inducing an immune response to a polypeptide in a subject, comprising administering the recombinant attenuated coxsackievirus B4 virion of claim 1 to the subject under conditions appropriate for infection by the virion.

55. *(withdrawn)*: A method for inducing an immune response to a polypeptide in a subject, comprising administering the recombinant attenuated coxsackievirus B4 virion CB4-P of claim 3 to the subject under conditions appropriate for infection by the virion.

56. *(withdrawn)*: The method of Claim 54 wherein the recombinant attenuated coxsackievirus B4 virion is formulated with a physiologically acceptable carrier.

57. *(currently amended/withdrawn)*: The method of Claim 54 wherein the immune response comprises the generation of a cytotoxic T-cell response, a T helper cell response, a B cell response, or any combination thereof.

58. *(withdrawn)*: The method of Claim 54 wherein the heterologous nucleic acid encodes a T-cell epitope.

59. *(withdrawn)*: A method for inducing an immune response to a polypeptide in a subject, comprising administering a recombinant attenuated CB4-P virion comprising the nucleic acid of claim 32 to the subject under conditions appropriate for infection by the virion.

60. *(previously amended/withdrawn)* : A method for inducing an immune response to a polypeptide in a subject, comprising administering the recombinant attenuated CB4-P virion of claim 7 to the subject under conditions appropriate for infection by the virion.

61. *(withdrawn)*: A method for inducing an immune response to a polypeptide in a subject, comprising administering the recombinant attenuated CB4-P virion of claim 14 to the subject under conditions appropriate for infection by the virion.

62. *(withdrawn)*: A method for inducing an immune response to a polypeptide in a subject, comprising administering the recombinant attenuated CB4-P virion of claim 15 to the subject under conditions appropriate for infection by the virion.

63. *(withdrawn)*: A method for inducing an immune response to a bacterial polypeptide in a subject, comprising administering a recombinant attenuated CB4-P virion comprising the heterologous nucleic acid of claim 34 to the subject under conditions appropriate for infection by the virion.

64. *(withdrawn)*: The method of Claim 63 wherein the immune response prevents or inhibits progression of a disease in the subject caused by bacteria comprising the heterologous bacterial polypeptide.

65. *(withdrawn)*: A method for inducing an immune response to a viral polypeptide in a subject, comprising administering a recombinant attenuated CB4-P virion comprising the nucleic acid of claim 33 to the subject under conditions appropriate for infection by the virion.

66. *(currently amended/withdrawn)*: The method of Claim 65 wherein the immune response prevents or inhibits progression of a disease in the subject caused by a virus comprising the heterologous viral polypeptide, wherein the heterologous viral polypeptide comprises a viral epitope.

67. *(currently amended/withdrawn)*: The method of Claim 65 wherein the immune response inhibits progression of the disease and the viral polypeptide is an HIV polypeptide or a peptide epitope fragment thereof.

68. *(currently amended/withdrawn)*: The method of Claim 67 wherein the HIV polypeptide is p24 or a peptide epitope fragment thereof.

69. *(withdrawn)*: The method of Claim 54 wherein the subject is human.

70. *(withdrawn)*: The method of Claim 54 wherein the subject is a nonhuman animal.

71. *(withdrawn)*: The method of Claim 54 wherein the subject is immunocompromised.

72. *(currently amended/withdrawn)*: A method for delivering a polypeptide to a subject, comprising administering to the subject, under conditions appropriate for infection, a recombinant attenuated coxsackievirus B4 virion which is engineered to comprise a heterologous nucleic acid insert that is inserted within the open reading frame of the coxsackievirus B4 genome, which insert encodes the polypeptide being delivered, which is

- (i) a heterologous ~~non-coxsackievirus~~ polypeptide fused to a capsid protein of the virion,
- (ii) expressed as an amino-terminal fusion with coxsackievirus B4 viral polyprotein; and
- (iii) susceptible to cleavage by a viral protease that cleaves the heterologous polypeptide from the viral polyprotein

thereby delivering the polypeptide.

73. *(new)* A recombinant attenuated coxsackievirus B4 virion consisting of a coxsackievirus B4 genome and a heterologous nucleic acid inserted within the P1 region of the open reading frame of the genome, which inserted nucleic acid encodes a heterologous polypeptide which is fused to a capsid protein of the virion.

74. (new) A recombinant attenuated coxsackievirus B4 virion which is engineered to contain a heterologous non-coxsackievirus nucleic acid inserted within the P1 region of the open reading frame of its genome, which inserted nucleic acid encodes a heterologous polypeptide which is fused to a capsid protein of the virion.

75. (new): A nucleic acid comprising the complete genome of a recombinant attenuated coxsackievirus B4 virion which is engineered to contain a heterologous non-coxsackievirus nucleic acid insert which is inserted within the P1 region of the open reading frame of its genome, wherein the insert encodes a heterologous polypeptide which in the virion is fused to a capsid protein.

76. (new): The recombinant attenuated coxsackievirus B4 virion of Claim 74 which is a CB4-P virion.

77. (new): The recombinant CB4-P virion of Claim 76 wherein the heterologous nucleic acid is expressed as an internal fusion of VP1.

78. (new): The recombinant CB4-P virion of Claim 76 wherein the heterologous nucleic acid is inserted in-frame and directly upstream of sequences which encode VP4, with the proviso that the insertion is optionally directly 3' from the AUG codon beginning at nucleotide 744 of the coxsackievirus B4 RNA genome that encodes the N-terminal Met of native viral polyprotein.